UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

SHIRE CANADA INC., SHIRE INTERNATIONAL LICENSING B.V., AND SHIRE US INC., Plaintiffs, v. BARR LABORATORIES, INC., Defendant.	**REDACTED** Civil Action No. 09-2380-PGG-KNF
SHIRE CANADA INC., SHIRE INTERNATIONAL LICENSING B.V., AND SHIRE US INC., Plaintiffs, v. MYLAN INC., MYLAN PHARMACEUTICALS INC., AND MATRIX LABORATORIES LIMITED, Defendants.	Civil Action No. 09-2555-PGG-KNF
SHIRE CANADA INC., SHIRE INTERNATIONAL LICENSING B.V., AND SHIRE US INC., Plaintiffs, v. NATCO PHARMA LIMITED, Defendant.	Civil Action No. 09-3165-PGG-KNF

DEFENDANTS' OPENING BRIEF IN SUPPORT OF CLAIM CONSTRUCTION

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

I. INTRODUCTION

Defendants Barr Laboratories, Inc. ("Barr"), Mylan Inc., Mylan Pharmaceuticals Inc., and Matrix Laboratories Limited ("Mylan"), and Natco Pharma Limited ("Natco") (collectively "Defendants") respectfully submit this opening brief in support of their proposed constructions of the disputed terms in the patents-in-suit: U.S. Patent Nos. 5,968,976 ("the '976 patent"), 7,465,465 ("the '465 patent"), and 7,381,428 ("the '428 patent"). All Defendants ask the Court to construe four terms in the '976 patent, and Defendants Barr and Natco also ask the Court to construe two terms in the '465 patent and eight terms in the '428 patent. A chart comparing Defendants and Shire's proposed constructions is attached as Exhibit 1.

II. THE LAW OF CLAIM CONSTRUCTION

Claim construction is a matter of law for resolution by the Court. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 372 (1996). In construing the claims, the Court should first consider the intrinsic evidence of record including the plain claim language, the specification, and the prosecution history. *Vitronics Corp. v. Conceptronic, Inc.,* 90 F.3d 1576, 1582 (Fed. Cir. 1996); *see also On Demand Mach. Corp. v. Ingram Indus., Inc.*, 442 F.3d 1331, 1337 (Fed. Cir. 2006) (citing *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc)).

The first source of evidence relevant to claim construction is the plain language of the claim itself. *Vitronics*, 90 F.3d at 1582. The context of a particular claim term at issue, both relative to other terms within that claim itself, as well as relative to terms used in other claims of the patent, is important to its construction. *Phillips*, 415 F.3d at 1314.

The second source of intrinsic evidence for claim construction is the specification, which "is always highly relevant to the claim construction analysis." *Phillips*, 415 F.3d at 1315 (internal citations and quotations omitted). "The specification acts as a dictionary when it

expressly defines terms used in the claims or when it defines terms by implication." *Vitronics*, 90 F.3d at 1582 (citation omitted). "Usually, [the specification] is dispositive; it is the single best guide to the meaning of a disputed term." *Phillips*, 415 F.3d at 1315. However, the specification cannot be used to expand a claim beyond the scope of the claim language. It is the claims of a patent, rather than the specification, that measure the patent right to exclude others. *Novo Nordisk of N.A., Inc., v. Genentech, Inc.*, 77 F.3d 1364, 1369 (Fed. Cir. 1996).

The third and final source of intrinsic evidence relevant to claim construction is the patent's prosecution history. The prosecution history informs the meaning of claim language by demonstrating how the inventor and the Patent Office understood the invention at the relevant time period. *Phillips*, 415 F.3d at 1317.

The Court may also consider extrinsic evidence. *See Phillips*, 415 F.3d at 1324; *Vitronics*, 90 F.3d at 1583. Sources of extrinsic evidence include prior art, dictionaries, treatises, and expert or inventor testimony. *Phillips*, 415 F.3d at 1317. Regardless of its type, extrinsic evidence is less significant than intrinsic evidence in determining the meaning of claim language, particularly extrinsic evidence that is contradictory to the intrinsic evidence. *Id.* at 1318; *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 862 (Fed. Cir. 2004); *Vitronics*, 90 F.3d at 1583.

III. THE '976 PATENT

The '976 patent claims pharmaceutical compositions comprising lanthanum carbonate, and methods for using those compositions, useful in treating patients with renal failure who develop a condition known as hyperphosphatemia. JA6[1:7–10].[1] Hyperphosphatemia is

[1] For the Court's convenience, the parties have compiled the evidence they cite in their claim construction briefs in a joint appendix. Joint appendix pages are cited as JA__. The format used to cite transcript and patent specification pages is JA__[page/column:line].

characterized by a relatively high concentration of phosphate in the blood. This condition occurs when conventional dialysis fails to reduce levels of phosphate in the blood, allowing phosphate levels to increase over time to undesirable levels. JA6[1:11–14].

Lanthanum carbonate has the chemical formula $La_2(CO_3)_3$. "La" is the chemical symbol for lanthanum; "CO_3" is the chemical formula for carbonate. The underlined number ( )$_{\underline{3}}$ in the formula $La_2(CO_3)_{\underline{3}}$ means that for every unit of lanthanum carbonate, there are three units of carbonate. According to this formula, one of ordinary skill in the art expects 3 moles of carbonate per mole[2] of lanthanum carbonate.[3] A general chemical term for this fixed relationship is "precise stoichiometry," which means that there is a fixed ratio per mole that determines the elemental composition of a chemical compound. REDACTED ; Declaration of Kim R. Dunbar, Ph.D. in Support of Defendants' Opening Claim Construction Brief (hereinafter "Dunbar") (attached as Exhibit 2), ¶ 16. Lanthanum carbonate can exist in forms containing water. Dunbar, ¶ 21. These compounds are referred to as lanthanum carbonate *hydrates* and are represented by the chemical formula $La_2(CO_3)_3 \cdot xH_2O$.

The specification of the '976 patent acknowledges that the prior art includes lanthanum carbonate octahydrate (*i.e.,* $La_2(CO_3)_3 \cdot 8H_2O$) and lanthanum carbonate monohydrate (*i.e.*, $La_2(CO_3)_3 \cdot H_2O$)[4] forms of hydrated lanthanum carbonate. The specification identifies

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[2] A "mole" is a convenient unit for chemists because individual molecules – for example, a single H_2O – are incredibly tiny. A mole is defined as 6.02×10^{23} molecules (which equals 602,000,000,000,000,000,000,000). REDACTED chemists commonly use the term mole and thus would say that there are three moles of carbonate per mole of lanthanum carbonate. JA7048[54:10-55:19]; Dunbar, ¶ 17.

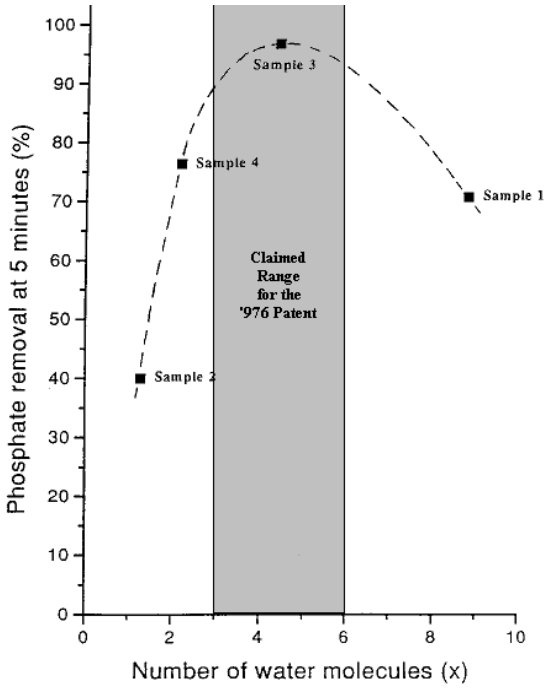
[3] REDACTED

[4] By convention, when x = 1, the number 1 is omitted from the chemical formula. *See, e.g.*, JA6[1:44–45] ("Example 11 of [JP 62-145024 ("Junji")] prepares $La_2(CO_3)_3 \cdot H_2O$, ie the monohydrate.").

lanthanum carbonate octahydrate (*i.e.*, x = 8) as being a commercially-available material. JA7[2:38–42]. The specification further identifies Japanese published patent application 62-145024, issued to Junji Nomura ("Junji"), as prior art and notes Junji discloses that "rare earth carbonates, bicarbonates, or organic acid compounds may be used as phosphate binding agents," this binding permitting phosphate removal. JA6[1:38–40]. Junji specifically discloses the use of one of the rare earth carbonates, lanthanum carbonate. JA6[1:37–47]. And Junji specifically discloses that a particular form of lanthanum carbonate, lanthanum carbonate *monohydrate*, was tested for its ability to bind and extract phosphate. JA6[1:37–47]; *see also* JA7013–14 & JA7003–07 (Junji disclosing a process for making lanthanum carbonate monohydrate and a method for using it to effectively treat patients with hyperphosphatemia).

The '976 inventors claim to have discovered that "certain forms of lanthanum carbonate exhibit improved performance in a variety of tests, over standard commercial lanthanum carbonate, which is believed to be the octahydrate form, and over [the monohydrate form] or similar compounds." JA6[1:48–52]. The only one of these "tests" reported in the '976 patent is a phosphate binding test, which the inventors allege "show[s] that certain lanthanum carbonate hydrates are significantly different in phosphate binding activity" from both lanthanum carbonate octahydrate and monohydrate, and other lanthanum carbonate hydrate forms. JA6[2:61–64].

The '976 inventors also state that the differences between the phosphate binding activity of the claimed forms of hydrated lanthanum carbonate and the "other forms," including the prior art octahydrate and monohydrate, is "readily seen from FIG. 1," which purports to show that "the highest phosphate removal is obtained with lanthanum carbonates having 3 to 6 molecules of water." JA7[3:43–46]; JA2[Fig. 1]. Figure 1 is reproduced below, with the "x" range of 3 to 6 water molecules highlighted.



JA2[Fig. 1] (shading added to show claimed range). In the figure above, Sample 3 (identified as having x = 4.4) falls within the range of x = 3 to 6, while Samples 1 (x = 8.8), 2 (x = 1.3), and 4 (x = 2.2) do not. JA6[2:38–55, 3:34–38]; JA2[Fig. 1]. The '976 patent further describes Samples 5 (x = 4) and 6 (x = 3.8) as falling within the range of 3 to 6 shown in Figure 1 above. JA7[3:36–38]. Thus the '976 inventors identified (and claimed) lanthanum carbonate hydrates with an "x" from 3 to 6 because these hydrates apparently have superior phosphate binding properties relative to the known monohydrate and octahydrate, as well as to the disclosed, but unclaimed, lanthanum carbonate dihydrate (x = 2.2).

The '976 patent describes the synthesis of Samples 2 (x = 1.3), 3 (x = 4.4), 4 (x = 2.2), and 6 (x = 3.8), and numerous other lanthanum carbonate samples having "x" values of 4.0 and 3.2 (Example 1), and 4.3, 4.6, and 4.0 (Example 2, these samples being combined and generally referred to as "4 H_2O" or tetrahydrate). JA7[3:59–4:65]. All of these samples are described as being prepared by drying higher hydrates of lanthanum carbonate including the octahydrate (Sample 1) which was dried to produce Samples 2–4. JA6–7[2:36–4:65]. In each case, the

reported value of "x" was determined by a method that can only be used to determine the average water content of the entire sample.[5] *See* Declaration of Harry G. Brittain, Ph.D., FRSC in Support of Defendants' Opening Claim Construction Brief (hereinafter "Brittain") (attached as Exhibit 3), ¶¶ 29–34.

The preparation described in the '976 patent is consistent with Great Britain Patent Application No. 9506126 ("GB '126") to which the '976 patent claims priority (the inventors were British). GB '126 explains that lanthanum carbonate "tetrahydrate" (*i.e.*, $La_2(CO_3)_3 \cdot 4H_2O$) was made by heating the lanthanum carbonate octahydrate (*i.e.*, x = 8) to make an amorphous solid. JA7026.

[6] REDACTED

[5] This is consistent with Defendants' proposed claim construction.

[6]

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A. The Claim Language of the '976 Patent Requiring Construction

1. Disputed Limitation: "lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$ where x has a value from" (claims 1–10)

One of the central disputes in this litigation concerns the meaning of a limitation appearing in all of the claims of the '976 patent – "lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$ where x has a value from . . . ." The claim phrase containing the formula $La_2(CO_3)_3 \cdot xH_2O$ also appears in claims of the '465 and '428 patents and it has the same meaning in all of the patents.

Defendants' Proposed Construction	Shire's Proposed Construction
the lanthanum carbonate present in the composition has an average water content equivalent to a water to $La_2(CO_3)_3$ mole ratio from	a crystalline form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate

The term "x" in $La_2(CO_3)_3 \cdot xH_2O$ should be construed to be an "average water content" of lanthanum carbonate present in a composition. This construction is consistent with the plain claim language, the specification, and file history of the '976 patent.

(a) The Plain Claim Language Supports Defendants' Construction.

The plain language of the claims of the '976 patent provides a sound basis for concluding the "x" value in the formula $La_2(CO_3)_3 \cdot xH_2O$ must be an "average" value of the total water content of the lanthanum carbonate composition. First, one of ordinary skill in the art would understand that the formula $La_2(CO_3)_3 \cdot xH_2O$ is an empirical formula representing a complex structure, not a single molecule. Brittain, ¶ 27. Thus, the "x" value in the formula represents the average mole ratio of water to lanthanum carbonate present in the lanthanum carbonate present in the structure. Brittain, ¶ 28. Second, the fact that several of the '976 claims recite the value of "x" as a non-integer value, *i.e.*, 3.5 and 3.8 to 4.5 (claims 2, 3, 8 and 9), rather than as a whole number value, *i.e.*, 3 to 6 (claim 1), would further evidence that the "x" values can only describe

an average value of the water content for a given amount of lanthanum carbonate. Brittain, ¶ 28; Dunbar ¶ 27.

(b) The '976 Patent Specification Also Supports Defendants' Construction.

In the '976 patent specification, three samples of $La_2(CO_3)_3 \cdot xH_2O$ (Samples 2–4 where x = 1.3, 4.4, and 2.2, respectively) are prepared by drying lanthanum carbonate octahydrate (x = 8.8). JA6[2:43–46]. Again, the use of non-integer values for "x" in connection with the samples informs one skilled in the art that "x" is an average value. Brittain, ¶ 28; Dunbar, ¶ 27. Moreover, the values of "x" reported in the table below for Samples 2–4 (col. 2 from the '976 patent) are calculated based on the weight of water lost by the *entire* sample during drying.

Sample	Initial wt (g)	Temp (° C.)	Time (min)	Vacuum (Y/N)	Wt loss (g)	x
2	5.00	175	240	Y	1.09	1.3
3	20.0	80	180	N	2.6	4.4
4	5.01	100	720*	N	0.96	2.2

*Dried to constant weight.

JA6[2:47–55] (table). One of ordinary skill in the art would understand that the weight loss information presented in the above table can only provide information regarding an *average* value of "x" representing the water content of the *entire* sample.[7] Brittain, ¶¶ 29–30;

[7] This table indicates the methodology used by the '976 inventors to determine the "x" value for a particular sample. Simply put, the method involves weighing the sample of starting material ($La_2(CO_3)_3 \cdot 8.8H_2O$) before drying, drying this material, and then subtracting the post-drying weight of the sample from the pre-drying weight of the sample to determine the weight loss during drying ("Wt loss (g)" in the foregoing table). The water lost (in grams) is then converted into moles of water lost due to drying. Having obtained the number of moles of water lost during drying, one subtracts this number from the moles of water in the sample prior to drying (*i.e.*, wherein x = 8.8) to obtain the value of "x" in the dried sample. Brittain, ¶¶ 29-30. One skilled in the art would understand this table to state that the loss of water upon drying of

Dunbar ¶¶ 33–34. This is because the water content – the "x" value – is calculated as the result of testing that tells one of skill in the art how much water is present in the entire sample after it is dried.[8] Dunbar, ¶¶ 33–34.

Examples 1 and 2 in the '976 patent also show that "x" is an average value of the entire sample of lanthanum carbonate tested. Brittain, ¶¶ 31–32; Dunbar, ¶¶ 33–34. Sample 6 in Example 1 and the unnumbered sample produced in Example 2 were both analyzed by drying the entire sample to determine the "x" value for the lanthanum carbonate hydrate tested. *Id.* In Examples 1 and 2, an unspecified hydrate of lanthanum carbonate was divided between three dishes and heated to remove water. JA7[4:7–28,7:36–58]; Dunbar, ¶¶ 33–34. The thermally-

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[8] the *entire* sample was used to determine the value of "x" in Samples 2, 3 and 4 (*i.e.*, wherein x = 1.3, 2.2 and 4.4, respectively) and therefore, "x" was an average. Brittain, ¶ 29–30.

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induced weight loss of each dish was monitored over time.[9] Dunbar, ¶¶ 33–34. In particular, Sample 6 referred to above was obtained by drying one portion of the initial lanthanum carbonate hydrate for 19.5 hours. JA7[4] (table, dish 1). The amount of water (*i.e.*, the "x" value) remaining in the samples for Example 1 after drying was calculated as a ratio of the number of moles of water per La (mol H_2O/La) after a certain number of hours and this data is shown in Figure 2.[10] JA7[4:26–27]; JA3[Fig. 2]. One skilled in the art would understand from these calculations of "x," which are based on water loss upon drying the samples over time, that "x" is an average value that can only reflect the total water content of the sample that was being tested. Brittain, ¶¶ 31–32; Dunbar, ¶¶ 33–34.

In Example 2, the samples were taken from three different drying dishes and *combined* before analyzing the weight of water lost due to drying. JA7[4:57–58]. Combining test samples from different dishes to be analyzed together shows that the inventors were not trying to determine the "x" value for individual particles contained in the test samples or the "x" value for individual test samples from a particular drying dish. Dunbar, ¶ 33. Instead, combining the dishes shows the inventors were only trying to determine the overall or average water content of all three dishes of dried material. Dunbar, ¶ 33. This conclusion is further supported by the way the inventors reported the value of "x" for samples from dishes 1–3. The inventors reported that these samples were "4H_2O" (or tetrahydrate) despite the fact that the individual dishes had "x"

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TGA is an analytical technique that measures the water lost in a sample as the temperature of that sample is increased. Dunbar, ¶¶ 28–34;

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[10] *See* JA6[2:28–30] & JA3[Fig. 2] ("Figure 2 illustrates the drying curves for five batches of lanthanum carbonate prepared by the method indicated in Example 1").

values of 4.3, 4.6, and 4.0 respectively for an average of x = 4.3 (as determined by thermal water loss methods) and an "x" value of approximately 3.8 (as determined by NMR).[11] JA7–8[4:45–67;5:4–5].

Figure 1 of the '976 patent further reinforces the conclusion that "x" is an average value of the entire tested sample. Figure 1 (shown above at p. 5) purports to show that lanthanum carbonate hydrates having an "x" value of 3 to 6 bind phosphate more rapidly and are thus more beneficial than lanthanum carbonate hydrates with an "x" value outside this range. However, none of the samples in Figure 1 correspond to precise stoichiometric hydrates of lanthanum carbonate – integers like 3, 4, or 5 – but rather the samples have the non-integer "x" values 8.8, 1.3, 4.4, and 2.2.[12] JA6[2:42, 2:51, 2:53]; JA7[3:35–36]; Dunbar, ¶ 27. The fact that non-integers are reported as the water content values for the samples listed in the '976 patent is a telltale sign that "x" is an average value. Brittain, ¶ 28; Dunbar, ¶ 27. Indeed, the '976 patent describes no way – other than averaging – to obtain the non-integer water content values for "x" as reported by the patent.

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[11] NMR, or nuclear magnetic resonance, is another analytical test that can provide only an average value for "x." Brittain, ¶ 31–32.

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(c) The File History Of The '976 Patent Also Supports Defendants' Construction.

Construing "x" as an average value also is consistent with the statements that Shire made to the U.S. Patent and Trademark Office ("USPTO") during prosecution. Specifically, when applying for a patent term extension, Shire explained that "[t]he active ingredient of FOSRENOL™ is lanthanum carbonate hydrate of the formula $La_2(CO_3)_3 \cdot xH_2O$, wherein x is *on average* 4.5, which falls within the ambit of the claims of U.S. Patent 5,968,976." JA271–72 (emphasis added). Further, when providing a complete identification of the approved product by chemical and generic name, Shire stated "[t]he approved product, FOSRENOL™, is a chewable tablet formulation containing, as the active ingredient, lanthanum carbonate hydrate. The lanthanum carbonate hydrate has the formula: $La_2(CO_3)_3 \cdot xH_2O$, wherein x is *on average* 4.5." JA272 (emphasis added). It is clear from these statements that Shire understood, and represented to the public, that the value of "x" in the formula $La_2(CO_3)_3 \cdot xH_2O$ is an average value for the entire amount of lanthanum carbonate included in the tablets. *See* JA271–72; Brittain, ¶ 35.

In addition, the '976 inventors characterized a number of prior art references disclosing lanthanum carbonate hydrates ($La_2(CO_3)_3 \cdot xH_2O$) as having various "x" values, *e.g.*, 5, 3 and 6. JA241–242; Brittain, ¶¶ 35–36. The only methods described in these prior art references to determine the value of "x" were methods that detected only the water content representing the average mole ratio of water to lanthanum carbonate for the entire sample. Brittain, ¶ 36. Thus, one of ordinary skill in the art would understand the inventors' statements to the USPTO to be a concession that the value of "x" recited by the '976 patent is a value that represents the average mole ratio of water to lanthanum carbonate for the entire amount of lanthanum carbonate included in a pharmaceutical composition (*e.g.*, a tablet). Brittain, ¶ 36.

(d) Shire's Proposed Construction Is Wrong.

Shire's proposed construction fails to acknowledge that the value of "x" must be an average value reflecting the average water content of the entire sample, in the form of a water to lanthanum carbonate mole ratio, as explained in detail above. In addition, Shire's proposed construction improperly limits "x" to specific crystalline forms of lanthanum carbonate hydrate. There is nothing in the plain language of the claims, the specification, or prosecution history of the '976 patent to support Shire's contention that the claim phrase should be understood to be limited to crystalline forms of lanthanum carbonate and thus to exclude non-crystalline or amorphous[13] forms of lanthanum carbonate. Nowhere is it described that the invention related to the use only of "crystalline" lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$.

To the contrary, the inventors of the '976 patent clearly intended that the lanthanum carbonate of the invention include non-crystalline or "amorphous" materials.[14] For example, GB '126, to which the '976 patent claims priority, describes the manner of making a lanthanum carbonate tetrahydrate (*i.e.,* $La_2(CO_3)_3 \cdot 4H_2O$) which GB '126 describes as an "amorphous solid." JA7026; *see also* Brittain, ¶ 42.

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The same Sample 5 described in the GB '126 priority application appears in the '976 patent. JA6[2:56–57]. This "amorphous" Sample 5 is identified by the inventors of the '976

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[13] A "crystalline" material is different from an "amorphous" material. Crystalline materials are more tightly ordered with regularly repeating chemical units and long range structural order. Dunbar, ¶¶ 18-20. By contrast, in amorphous materials the structure of the chemical units is more random without long range structural order. *Id.*

[14] REDACTED

patent as one of three samples (*i.e.*, Samples 3, 5, and 6) that acted as "fast" phosphate binders (s*ee* Table 1) in the very binding study the inventors carried out to demonstrate the apparently superior properties of lanthanum carbonate hydrates having the claimed "x" value of from 3 to 6. JA7[3:20–42].

The identification of this *amorphous* tetrahydrate in the '976 patent as a preferred lanthanum carbonate hydrate contradicts Shire's proposed construction. It demonstrates that the inventors considered amorphous lanthanum carbonate hydrates to fall within the scope of the claimed invention. Brittain, ¶ 42. Since Shire's proposed construction is contradicted by the intrinsic evidence, it must be rejected in favor of Defendants' proposed construction, which encompasses all lanthanum carbonate hydrates, crystalline or amorphous.

Accordingly, Defendants respectfully request that the Court adopt their proposed construction.

2. Disputed Limitation: "a pharmaceutical composition for the treatment of hyperphosphataemia" (claim 1)[15]

Defendants' Proposed Construction	Shire's Proposed Construction
a pharmaceutical composition wherein the amount of $La_2(CO_3)_3 \cdot xH_2O$ present in the composition is effective to treat hyperphosphatemia	therapeutic mixture (i.e., one which is sterile, reasonably safe and non-toxic) suitable for administration into the gastrointestinal tract for the treatment of hyperphosphatemia

Defendants submit that this claim phrase, as properly construed, requires that the claimed pharmaceutical composition contain not just any amount of $La_2(CO_3)_3 \cdot xH_2O$, but an amount that is effective to treat hyperphosphatemia. Brittain, ¶¶ 72–76. This proposed construction is supported by the specification and prosecution history of the '976 patent, which each make clear

[15] The word "hyperphosphatemia" is spelled "hyperphosphataemia," with an extra "a," in the in the '976 patent. There is no difference in meaning between these two spellings. Defendants use the spelling "hyperphosphatemia" in this brief except when quoting.

that the invention described by this claim language is not just any amount of lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$ (x = 3–6), but is an amount that is effective to treat hyperphosphatemia.

(a) The '976 Patent Specification Supports Defendants' Construction.

The specification of the '976 patent describes a method of treating hyperphosphatemia by administering "an effective dose of [] lanthanum carbonate into the gastrointestinal tract." JA6[1:64–67]. However, the specification does not refer to, and the patent does not claim, all lanthanum carbonate hydrate forms. *See* JA6[1: 53–58, 64–67]. The only lanthanum carbonate hydrates claimed by the '976 patent are lanthanum carbonate hydrates with an average water content of 3 to 6 moles or, in other words, $La_2(CO_3)_3 \cdot xH_2O$ where "x" is 3 to 6. JA6[1:53–58]. The specification clearly relates therapeutic efficacy to the amount of the lanthanum carbonate hydrate of the formula $La_2(CO_3)_3 \cdot xH_2O$ (in this case, wherein "x" is from 3 to 6) in the composition or dose. It would be improper to construe the claims to cover a pharmaceutical composition that contains less than a therapeutic amount of a lanthanum carbonate hydrate having the formula $La_2(CO_3)_3 \cdot xH_2O$ (with "x" having the value specified in the particular claim). Brittain, ¶¶ 72–75.

(b) The '976 Patent File History Also Supports Defendants' Construction.

The prosecution history further supports Defendants' construction of this claim term. Brittain, ¶ 76. The inventors described their invention to the USPTO during the prosecution consistent with the specification. The inventors characterized their invention as "the unexpected discovery that lanthanum carbonates with waters of crystallization or hydration between 3 and 6 moles of water per mole of lanthanum carbonate are particularly effective in absorbing phosphate both *in vivo* and *in vitro*." JA238. Thus, the inventors indicated quite clearly that

lanthanum carbonate hydrate (*i.e.*, $La_2(CO_3)_3 \cdot xH_2O$ where "x" is 3 to 6) must be present in the pharmaceutical composition, not just in any amount, but in an amount effective to treat hyperphosphatemia. Brittain, ¶ 76.

(c) Shire's Proposed Construction Is Wrong.

Shire's construction is ambiguous. It fails to specify what active ingredient is required to be present in an amount sufficient to produce the claimed therapeutic effect. Brittain, ¶¶ 73–74.

Accordingly, Defendants respectfully request that the Court adopt their proposed construction.

3. Disputed Limitation: "effective to treat said hyperphosphataemia" (claim 7)

Defendants' Proposed Construction	Shire's Proposed Construction
wherein the amount of $La_2(CO_3)_3 \cdot xH_2O$ present in the composition is effective to treat hyperphosphatemia	capable, without toxic effects, of maintaining the serum phosphate level of a subject at a substantially constant level or reducing the serum phosphate level in a subject who has an excess level of serum phosphate

With respect to the claim phrase "effective to treat said hyperphosphataemia," Defendants' proposed construction is similar to the construction proposed for the phrase "a pharmaceutical composition for the treatment of hyperphosphataemia." The amount of $La_2(CO_3)_3 \cdot xH_2O$ (where x = 3 to 6) contained in the claimed composition may not be any amount, but must be an amount effective to treat hyperphosphatemia. As before, Defendants' construction is supported by the specification and the file history for the reasons explained above in Sections III.A.2.a & b. *See also* Brittain, ¶ 77. Shire's proposed construction is incorrect because it fails to clearly relate the therapeutic effect to the amount of lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$ present in the composition as explained in Section III.A.2.c. *See also* Brittain, ¶ 78. The plain language of claim 7, in which this claim phrase appears, also supports Defendants' proposed construction.

(a) The Plain Claim Language Supports Defendants' Construction.

The plain language of claim 7 recites a method for treating hyperphosphatemia in a subject by administering "*an amount of lanthanum carbonate of the formula* $La_2(CO_3)_3 \cdot xH_2O$ . . . [that is] *effective to treat* [] hyperphosphataemia." JA8[6:39–46] (emphasis added); Brittain, ¶ 77.

Defendants therefore respectfully request that the Court adopt their proposed construction.

4. Disputed Limitation: "in unit dosage form to provide from 0.1 to 20 g/day" (claim 4)

Defendants' Proposed Construction	Shire's Proposed Construction
one or more unit dosage forms to provide a total daily dose of from 0.1 to 20 g/day of $La_2(CO_3)_3 \cdot xH_2O$	a solid or liquid form used to administer a dose of between 0.1 and 20 g/day of elemental lanthanum

All of the parties appear to recognize that the claim phrase "in unit dosage form to provide from 0.1 to 20 g/day," which appears in claim 4 of the '976 patent, is unclear because it fails to specify to what the numerical range of "0.1 to 20 g/day" refers. Brittain, ¶ 68. The Court should adopt Defendants' construction because it is consistent with the specification. Shire's proposed construction should be rejected because it is unsupported by the specification of the '976 patent.

(a) The '976 Patent Specification Supports Defendants' Construction.

The specification explains that the invention includes the administration of an effective dose of *lanthanum carbonate* into the gastrointestinal tract, and further describes experiments where rats were dosed with an amount of $La_2(CO_3)_3 \cdot 4H_2O$. JA6[1:64–67]; JA8[5:30–37]; Brittain, ¶ 69. The unit dose the invention requires is a unit dose of lanthanum carbonate. JA6[1:64–67]; JA8[5:30–37]. And one of ordinary skill in the art would know that a "unit

dosage form to provide from 0.1 to 20 g/day" is a unit dose of lanthanum carbonate. Brittain, ¶ 67.

Further, one of ordinary skill in the art would understand that the claim phrase must mean "one or more unit dosage forms" can be administered to provide the recited daily dose. Brittain, ¶ 70. This is because one of ordinary skill in the art would understand that it is impossible to administer 20 g (40 times the common 500mg unit dosage size) to a patient in a single unit dosage form. Brittain, ¶ 68.

(b) Shire's Proposed Construction Is Wrong.

Contrary to the '976 patent specification, Shire's proposed construction requires a dose of "elemental lanthanum" (*i.e.*, an amount of La). The specification fails to include any discussion whatsoever regarding "elemental lanthanum," let alone a discussion of the daily dose of elemental lanthanum to be administered to a patient. Brittain, ¶ 69. Shire's construction should be rejected.

Accordingly, Defendants respectfully request that the Court adopt the construction proposed by Defendants.

IV. THE '465 PATENT

The '465 patent claims chewable pharmaceutical compositions that contain lanthanum carbonate compounds. Shire filed this patent years after the '976 patent issued and identified the '976 patent as prior art. JA14[1:26–30]. The two patents cover substantially similar technology. Both patents claim the administration of lanthanum carbonate formulations to treat hyperphosphatemia. In relevant part, the '465 patent requires, *inter alia*, that the claimed formulation be in a chewable or powder form, contain certain inactive ingredients, and be prepared by specific processes. JA14[1–2]. The '465 patent describes the preferred embodiment

of the invention as "lanthanum carbonate of the general formula: $La_2(CO_3)_3 \cdot xH_2O$ where . . . most preferably x has an average value of 4," but allows "x" to range from 3 to 8, and incorporates the '976 patent by reference. JA15[4:11–23]. The '465 patent specification further states that "the hydration level of the lanthanum compound can be measured by methods well known in the art, such as thermal analysis (TGA)." JA15[2:23–25]. Like the '976 patent, the '465 patent never requires that the lanthanum carbonate exist as a crystalline structure.

A. The Claim Language of the '465 Patent Which Requires Construction

1. Disputed Limitation: "lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$ where x has a value from" (claims 3 and 4)

Defendants' Proposed Construction	Shire's Proposed Construction
the lanthanum carbonate present in the composition has an average water content equivalent to a water to $La_2(CO_3)_3$ mole ratio from	a crystalline form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate

The '976 patent and the '465 patent both contain this claim limitation. The parties have proposed the same construction for this limitation in connection with each patent. As explained in detail above, one of ordinary skill in the art would, and thus this Court should, adopt Defendants' construction because the construction reflects the plain language of the claims, the teachings in the specification, and the prosecution history. *See discussion at Section III.A.1*; Brittain, ¶ 46. The '465 patent specifically incorporates the '976 patent by reference; therefore, the same language and arguments that support the Defendants' proposed construction of this term in the '976 patent equally apply here and will not be repeated. *See Section III.A.1.*

(a) The '465 Patent Specification Supports Defendants' Construction.

Consistent with teachings in the '976 patent (which the '465 inventors incorporated by reference), the '465 patent specification lends further support to Defendants' proposed

construction. The '465 patent refers to "x" as a non-integer value (i.e., x = 3 to 4.5 or "most preferably 3.4"). JA15[4:11–19]. As discussed above, one of ordinary skill in the art would understand that references to non-integer "x" values can only describe an average value of the water content because water content is determined by techniques that can only provide the total water content and not any type of speciation. *See Section III.A.1.a*; Brittain, ¶ 48.

Furthermore, the '465 patent specification never describes the lanthanum carbonate samples as mixtures of stoichiometric lanthanum carbonate hydrates. *See Section III.A.1.b*; Brittain, ¶ 49. These teachings consistently support the adoption of Defendants' position that "x" represents an average water content in both the '465 patent and the '976 patent.

The test method disclosed in the '465 patent for determining "x" also supports Defendants' position that "x" should be construed as an average water content. The '465 patent specification teaches that "methods well known in the art, such as thermal analysis (TGA)" should be used to determine "x." JA15[4:23–25]. It is known in the art that TGA only provides an average value for "x" based on the entire sample being tested. Brittain, ¶ 49. The specification does not include or suggest any other analytical technique for calculating "x," much less one capable of identifying a stoichiometric hydrate in a tested sample. Significantly, nothing in the '465 patent specification would lead one of ordinary skill in the art to understand "x" as anything other than an average value of the ratio of water to lanthanum carbonate in the entire lanthanum carbonate hydrate sample. Brittain, ¶ 49. Accordingly, Defendants respectfully request that the Court adopt their proposed construction.

2. Disputed Limitation: "lanthanum carbonate is hydrated having a water content of about 4 moles of water" (claims 7 and 8)

Defendants' Proposed Construction	Shire's Proposed Construction
the lanthanum carbonate present in the composition has an average water content equivalent to a water to $La_2(CO_3)_3$ mole ratio of about 4	lanthanum carbonate present in the tablet has a ratio of approximately 4 moles of water to one mole of lanthanum carbonate

A person of ordinary skill in the art would understand the claim phrase "the lanthanum carbonate is hydrated having a water content of about 4 moles of water," which appears in claims 7 and 8 of the '465 patent, to have the same meaning as the claim phrase "lanthanum carbonate of the formula: $La_2(CO_3)_3 \cdot xH_2O$ where x has a value from" discussed above. *See also* Brittain, ¶¶ 50–52.

(a) The '465 Patent Specification Does Not Define "Water Content."

The specification of the '465 patent contains no single reference to the "water content" of lanthanum carbonate. Nor does the specification describe a lanthanum carbonate that is "hydrated having a water content of about 4 moles of water." Brittain, ¶ 51. Outside of arguments the inventors made during prosecution of the '465 patent, the specification provides little insight into how this limitation should be construed.

(b) The '465 Patent File History Supports Defendants' Constructions.

The prosecution history provides strong support for Defendants' proposed construction. As filed, neither the '465 patent specification or claims made any reference to the "water content" of lanthanum carbonate. Brittain, ¶ 51. The inventors first introduced this language through an amendment in response to the first office action. JA1910; *see also* Brittain, ¶¶ 51–52. Specifically, the inventors amended the application to include new claims 50 and 51, which later issued as claims 7 and 8. JA1910. The inventors identified the portion of the specification that teaches "x" in $La_2(CO_3)_3 \cdot xH_2O$ can range from 3 to 8 as support for the new claim language.

JA1912–13 (citing the specification at JA15[4:11–19]); *see also* Brittain, ¶¶ 51–52. By doing so, the inventors advised one of ordinary skill and the public that the claim phrase "the lanthanum carbonate is hydrated having a water content of about 4 moles of water" has the same meaning as the claim phrase "lanthanum carbonate of the formula: $La_2(CO_3)_3 \cdot xH_2O$ where x has a value from." Brittain, ¶ 52. The limitation should be construed consistently with the inventors' arguments during prosecution, which requires "x" to cover an average water content (*i.e.*, the average ratio of one mole of lanthanum carbonate to "x" moles of water).

V. THE '428 PATENT

The '428 patent claims methods of using lanthanum carbonate compositions stabilized against "substantial decarboxylation to lanthanum hydroxycarbonate" by the presence of one or more mono- or disaccharides excipients after the composition is exposed to specific heat and moisture stress conditions. JA48[17:39–60,18:20–39]. Like its parent, the '465 patent, the '428 patent claims the administration of lanthanum carbonate formulations to treat hyperphosphatemia (see claim 1) and identifies the '976 patent as prior art. JA40[1:44–47]. The claims of the '428 patent also require that the amount of lanthanum carbonate administered be effective to treat hyperphosphatemia. JA48[17:39–45].

The '428 patent describes that when lanthanum carbonate is formulated with mono- or disaccharides (*i.e.*, inactive excipients), it is "stabilized" such that degradation of the lanthanum carbonate by decarboxylation to an impurity called "lanthanum hydroxycarbonate" is prevented or reduced. JA41–42[3:48–59,4:61–5:6]. The impurity lanthanum hydroxycarbonate can be detected by x-ray powder diffraction ("XRPD"). JA42[5:18–24]. XRPD is an analytical testing technique that can, in certain cases, be used to generate a "pattern" of peaks to compare the material tested to a known XRPD reference pattern. Brittain, ¶ 60. The '428 patent specification

describes that certain peaks are characteristic for "lanthanum hydroxycarbonate" in an XRPD pattern and no hydroxycarbonate is detected in a sample when those peaks are not observed in the XRPD pattern of the sample tested. JA42[5:18–24]; JA46–47[13:60–16:67].

A. The Claim Language of the '428 Patent Requiring Construction

1. Disputed Limitation: "lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$ where x has a value from" (claims 1–3 and 7–9)

Defendants' Proposed Construction	Shire's Proposed Construction
the lanthanum carbonate present in the composition has an average water content equivalent to a water to $La_2(CO_3)_3$ mole ratio from	a crystalline form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate, wherein x has a value from

All three of the patents-in-suit contain this claim limitation. The parties have proposed the same construction for the limitation in connection with each of the three patents. Defendants have explained that "x" refers to the *average* water content of the entire sample of lanthanum carbonate present in a pharmaceutical composition (*e.g.*, a tablet). As explained in detail above, one of ordinary skill in the art would, and thus this Court should, adopt Defendants' construction because the construction reflects the plain language of the claims, the teachings in the specification, and the prosecution history. *See discussion at Section III.A.1*; Brittain, ¶¶ 57–66. And because the '428 patent specifically incorporates the '465 patent by reference, which in turn incorporates the '976 patent by reference, the same language and arguments that support the Defendants' proposed construction of this term in the '976 and '465 patents equally apply here and will not be repeated. *See Sections III.A.1 and IV.A.1*.

(a) The '428 Patent Specification Supports Defendants' Construction.

The '428 patent explains that the stabilized compositions of the invention contain lanthanum carbonate having the general formula $La_2(CO_3)_3 \cdot xH_2O$. Nothing in the '428 patent

describes the lanthanum carbonate samples as mixtures of stoichiometric lanthanum carbonate hydrates having discrete values of "x." *See Section III.A.1*; Brittain, ¶ 61. To the contrary, the '428 patent states that "[m]ost preferably, x may have *an average* value of about between 4 and 5." JA41[4:35–40] (emphasis added); *see also* Brittain, ¶ 63. This reinforces Defendants' proposed construction that "x" is, and would be understood by one of ordinary skill in the art to be, an *average* value representing the ratio of the number of moles of $La_2(CO_3)_3$ to the number of moles of water. Brittain, ¶¶ 59–61.

The '428 patent further teaches that the "hydration level of the lanthanum compound [(*i.e.*, the value of 'x')] can be measured by methods well known in the art, such as [by] thermogravimetric analysis (TGA) or x-ray powder diffraction (XRPD)." JA41[4:39–44]. As discussed above in the context of the '976 patent, thermal methods such as TGA can only provide information about the average value of "x" for the entire sample tested. Brittain, ¶ 59. While XRPD is also mentioned as a technique for determining "hydration level" (*i.e.*, "x"), one of ordinary skill in the art would understand that XRPD is only useful to determine "x" to the extent that reference patterns for various values of "x" are available for comparison. Brittain, ¶¶ 59–60. While the '428 patent includes XRPD patterns for a lanthanum carbonate tetrahydrate (*i.e.*, $La_2(CO_3)_3$•4–5H_2O), the '428 patent does not disclose reference patterns for other hydrates, such as lanthanum carbonate dihydrate or octahydrate. Thus one of ordinary skill in the art would know that XRPD has limited value to determine "x" in the context of the '428 patent. *See* Brittain, ¶ 60.

(b) The '428 Patent File History Also Supports Defendants' Construction.

During prosecution, the inventors of the '428 patent equated "x" in the formula $La_2(CO_3)_3$•xH_2O to the average water content of the claimed lanthanum carbonate composition.

JA4879–80. Specifically, the inventors provided an illustration of how to calculate the percentage amount of elemental lanthanum in composition comprising hydrated lanthanum carbonate "having a water content approximately equivalent to 4–5 moles of water." JA4879–80; JA4887–88. These calculations demonstrate that the inventors of the '428 patent understood "x" to refer to an average water content reflecting a water to lanthanum carbonate mole ratio for the hydrated lanthanum carbonate contained in the composition. JA4879–80; JA4887–88; Brittain, ¶ 64.

Accordingly, Defendants respectfully request that the Court adopt their proposed construction.

2. Disputed Limitation: "lanthanum carbonate has a *water content* approximately equivalent to 4–5 moles of water" (claims 4–6, 10–12)[16]

Defendants' Proposed Construction	Shire's Proposed Construction
the lanthanum carbonate present in the composition has an average water content approximately equivalent to a water to $La_2(CO_3)_3$ mole ratio of 4–5	"water content" means "ratio of moles of water to one mole of lanthanum carbonate"

The phrase "lanthanum carbonate has a water content approximately equivalent to 4–5 moles of water" in claims 4–6 and 10–12 of the '428 patent is very similar to the phrase "lanthanum carbonate is hydrated having a water content of about 4 moles of water" recited in claims 7 and 8 of the '465 patent. One of ordinary skill in the art would understand both phrases to have the same meaning as the claim phrase "lanthanum carbonate of the formula

[16] Shire asserts that the term "water content" as used in claims 4–6 and 10–12 requires construction by the Court. Defendants believe that the term "water content" cannot be properly construed apart from the entire phrase "lanthanum carbonate has a *water content* approximately equivalent to 4–5 moles of water." Brittain, ¶ 66.

$La_2(CO_3)_3 \cdot xH_2O$ where x has a value from" discussed immediately above in Section V.A.1, and in Section III.A.1 relative to the '976 patent. Brittain, ¶¶ 62–63, 65–66.

(a) The Plain Claim Language Supports Defendants' Construction.

The plain language of the claim requires "lanthanum carbonate [that] has a water content approximately equivalent to 4–5 moles of water." In other words, the claim requires that the "water content" of the claimed composition have on average one mole of $La_2(CO_3)_3$ for every "4–5 moles of water." Brittain, ¶ 62.

(b) The Prosecution History Supports Defendants' Construction.

As discussed above, the inventors equated "x" in the formula $La_2(CO_3)_3 \cdot xH_2O$ to the average water content of the claimed lanthanum carbonate composition during prosecution of the '428 patent. JA4879–80. Specifically, the inventors determined the percentage amount of elemental lanthanum present in a composition containing "hydrated lanthanum carbonate having a water content approximately equivalent to 4–5 moles of water," as referenced in Example 5, by treating the "water content" value 4–5 moles as equivalent to an "x" value of 4 to 5. JA4879–80; JA4887–88. There can be no doubt that the inventors viewed "x" as equivalent to the average water content of the lanthanum carbonate sample. Brittain, ¶ 64.

Defendants therefore respectfully request that the Court adopt their proposed construction.

3. Disputed Limitations: "therapeutically effective amount" and "amount effective to treat hyperphosphatemia" (claims 1–6)

Defendants' Proposed Construction	Shire's Proposed Construction
the amount of $La_2(CO_3)_3 \cdot xH_2O$ present in the composition is effective to treat hyperphosphatemia	amount or dose [of lanthanum carbonate] sufficient (i) to detectably decrease the serum phosphate levels of a subject or (ii) at a minimum, to keep the serum phosphate levels of a subject substantially constant

A person of ordinary skill in the art would understand that the claim phrases "therapeutically effective amount" and "amount effective to treat hyperphosphatemia" require that the *amount* of $La_2(CO_3)_3 \cdot xH_2O$ in the claimed composition be effective to treat hyperphosphatemia. Brittain, ¶ 79. This construction is supported by the plain language of these claim phrases as well as the '428 patent specification. Brittain, ¶¶ 79–83.

(a) The Plain Claim Language Supports Defendants' Constructions.

The plain language of the claims require a "therapeutically effective amount of a lanthanum carbonate composition" containing $La_2(CO_3)_3 \cdot xH_2O$ in "an amount effective to treat hyperphosphatemia." JA48[17:39–40,45–46]. Based on this language, one of ordinary skill in the art would understand that the amount of the claimed lanthanum carbonate hydrate active ingredient in the composition (*i.e.*, the $La_2(CO_3)_3 \cdot xH_2O$) must be effective to treat hyperphosphatemia. Brittain, ¶ 82.

(b) The '428 Patent Specification Also Supports Defendants' Proposed Construction.

The specification explains that "[i]n accordance with the present invention, a stabilized lanthanum carbonate composition is provided, comprising a *pharmaceutically effective amount of lanthanum carbonate* having the general formula $La_2(CO_3)_3 \cdot xH_2O$." JA40[1:63–66]; Brittain, ¶ 81. The specification also states that a "pharmaceutically effective amount" or a "therapeutically effective amount" is "an amount or dose sufficient (i) to detectably decrease the serum phosphate levels of a subject or (ii) at a minimum, to keep the serum phosphate levels of a subject substantially constant." JA41[4:1–6]. Although the specification purports to define these claim phrases, one of ordinary skill in the art would interpret the claim phrases in context of the language that surrounds them. The words of the specification make clear that the "pharmaceutically effective amount of lanthanum carbonate" is a pharmaceutically effective

amount of the $La_2(CO_3)_3 \cdot xH_2O$. And the plain language of claim 1 requires that the "therapeutically effective amount" of $La_2(CO_3)_3 \cdot xH_2O$ be "effective to treat hyperphosphatemia." JA48[17:39–46]. Accordingly, the "therapeutically effective amount" is merely an *amount* of $La_2(CO_3)_3 \cdot xH_2O$ that is effective to treat hyperphosphatemia. Brittain, ¶¶ 80–83.

(c) Shire's Proposed Constructions Are Wrong.

Confusingly, Shire's proposed constructions fixate on the specification's definition of "therapeutically effective amount" and appear to require testing the "phosphate levels of a subject" after a dose of a lanthanum carbonate composition is administered. However, Shire's construction ignores that the claim language requires only that the *amount or dose* of $La_2(CO_3)_3 \cdot xH_2O$ be effective to treat hyperphosphatemia – the claim language does not require the additional step of testing the "phosphate levels of a subject." Brittain, ¶¶ 79–82.

Defendants' proposal provides the construction that is most consistent with the claim language and specification; it should be adopted.

4. Disputed Limitations: "stabilizing the lanthanum carbonate against substantial decarboxylation to lanthanum hydroxycarbonate" (claims 1–6) and "the lanthanum carbonate being stabilized against substantial decarboxylation to lanthanum hydroxycarbonate" (claims 7–12)

Defendants' Proposed Construction	Shire's Proposed Constructions[17]
stabilizing the lanthanum carbonate present in the composition such that no lanthanum hydroxycarbonate formed by decarboxylation of the lanthanum carbonate is detectable in an	retarding the lanthanum carbonate [in which the lanthanum carbonate is retarded] from degrading into lanthanum hydroxycarbonate in an amount sufficient so that a skilled

[17] The parties' propose constructions for these two claim phrases that are identical (in the case of Defendants) or nearly identical (in the case of Shire). The minor variation in Shire's proposed construction for the claim phrase in claim 7 relative to claim phrase in claim 1 is bracketed in the text of Shire's proposed construction.

x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate composition after the composition has been exposed to 60° C and 95% relative humidity for at least 7 days, wherein lanthanum hydroxycarbonate is a species characterized by the four peaks identified by "HC" in the x-ray powder diffraction pattern appearing in Figure 13 for t = 7 days	artisan detects lanthanum hydroxycarbonate through visual inspection of an x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate composition after it has been exposed to 60° C. and 95% relative humidity for at least 7 days

These disputed claim phrases consist of three parts that must be construed. First, the term "lanthanum hydroxycarbonate" should be defined to mean the lanthanum hydroxycarbonate identified by the '428 patent specification as "a species characterized by the four peaks identified by 'HC' in the x-ray powder diffraction pattern appearing in Figure 13 for t = 7 days." Second, the phrase "stabilizing . . . against substantial decarboxylation" should be defined according to the definition offered by the inventors during prosecution to mean that "no lanthanum hydroxycarbonate formed by decarboxylation of the lanthanum carbonate is detectable in an x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate composition after the composition has been exposed to 60°C and 95% relative humidity for at least 7 days." Third, the claim phrase should be construed so as to make clear that no "lanthanum hydroxycarbonate" is formed as a result of decarboxylation of the lanthanum carbonate present in the composition after exposure to the claimed stress conditions, and that the claims do not encompass lanthanum hydroxycarbonate already present in the composition prior to exposure to the stress conditions. Brittain, ¶¶ 84–85.

(a) Part One: "lanthanum hydroxycarbonate."

One skilled in the art would recognize that the XPRD pattern shown in Figure 13 of the '428 patent specification identifies the species of "lanthanum hydroxycarbonate" required by claims 1 and 7. Brittain, ¶¶ 85, 92–94; *see also* JA37[Fig. 13]. This definition of "lanthanum hydroxycarbonate" is required because one skilled in the art at the time the '428 patent was filed

would know that "lanthanum hydroxycarbonate" could encompass multiple forms of lanthanum hydroxycarbonate including polymorphs and amorphous forms. Brittain, ¶ 92. Claims 1 and 7, however, require a specific species of lanthanum hydroxycarbonate formed after exposure to the claimed stress conditions of "60° C. and 95% relative humidity for at least 7 days." JA48[17:59–60,18:39–40]. This species of "lanthanum hydroxycarbonate" is identified by the '428 patent specification as the species having the four peaks marked as "HC" in the XRPD pattern labeled Figure 13 for t = 7 days. Brittain, ¶¶ 93–94; *see also* JA41[3:55–59] (explaining that the claimed "stabilized" lanthanum carbonate composition "degrades into lanthanum hydroxycarbonate at a slower rate compared to lanthanum carbonate alone or not in the presence of other materials"); JA37[Fig. 13]. The selection of Figure 13 is appropriate because it sets forth the XRPD pattern observed for lanthanum carbonate "not in the presence of" a monosaccharide or disaccharide stabilizer following exposure to the claimed stress conditions of "60° C. and 95% relative humidity for at least 7 days." Brittain, ¶¶ 92–94; *see also* JA37[Fig. 13].

(b) Part Two: "stabilizing . . . against substantial decarboxylation."

During prosecution, the inventors amended the claims that ultimately issued as claims 1 and 7 to require that the "stabilized" lanthanum carbonate composition contain a mono- or disaccharide stabilizer "in an amount sufficient to stabilize the lanthanum carbonate against substantial decarboxylation to lanthanum hydroxycarbonate." JA2669 (filed claim 13 ultimately issued as claim 1 of the '428 patent). The USPTO rejected these claims because the phrase "against substantial decarboxylation" was unclear. JA4447–48. In response, the inventors amended the claims further to define stabilization against "substantial decarboxylation" as requiring an "amount of [] stabilizer [] such that lanthanum hydroxycarbonate is not observed in an . . . [XRPD] pattern of the lanthanum carbonate and the stabilizer after the lanthanum carbonate and the stabilizer have been exposed to 60° C. and 95% relative humidity for 7 days."

JA4666; JA4671. The inventors' amendments during prosecution make clear that stability against "against substantial decarboxylation" requires that "no lanthanum hydroxycarbonate formed by decarboxylation of the lanthanum carbonate is detectable in an XRPD pattern of the lanthanum carbonate composition after the composition has been exposed to 60°C and 95% relative humidity for at least 7 days." Brittain, ¶¶ 85, 89.

(c) Part Three: the lanthanum hydroxycarbonate referenced in the claim phrases is lanthanum hydroxycarbonate formed as a result of decarboxylation of the lanthanum carbonate present in the composition.

The '428 patent specification makes clear that the invention is a lanthanum carbonate composition "stabilized" by one or more mono- or disaccharides, where the stabilization prevents formation of any new "lanthanum hydroxycarbonate" by decarboxylation *after* the composition is exposed to heat or moisture stress conditions. JA41[3:48–52]. The specification explains that in the "stabilized" composition lanthanum carbonate "degrades into lanthanum hydroxycarbonate at a slower rate compared to lanthanum carbonate alone or not in the presence of other materials." JA41[3:55–59]. Thus, these claim phrases identify a composition where lanthanum carbonate is protected against *further* decarboxylation, not a composition that merely contains no lanthanum hydroxycarbonate. Brittain, ¶¶ 85–86, 95.

(d) Shire's Proposed Construction Is Wrong.

Detection of lanthanum hydroxycarbonate is not limited to "visual inspection" of an XRPD pattern, as Shire argues. Indeed, the phrase "visual inspection" does not appear anywhere in the '428 patent's claims or specification. Brittain, ¶ 91. And in contrast to Shire's proposed construction, the plain language of claims 1 and 7 requires that "lanthanum hydroxycarbonate is not *observed*" in the XRPD pattern of the tested sample. JA48[17:57–58,18:35–36]. The specification explains that "the absence of observable peaks indicates no *detectable*

degradation," JA42[5:18–24], and teaches that an amount of mono- or disaccharides retards degradation of lanthanum carbonate so that "substantially no *detectable* degradation occurs." JA41–42[4:61–5:6]. One skilled in the art would know that any technique available at the time the '428 patent was filed could be used to "observe" peaks in an XRPD pattern and "detect" lanthanum hydroxycarbonate in a sample after it is exposed to the claimed stress conditions. Brittain, ¶ 91.

Shire's proposed construction is also flawed because it fails to define lanthanum hydroxycarbonate or to make clear that the claims require that no lanthanum hydroxycarbonate be formed by decarboxylation of the lanthanum carbonate present in the composition *after* it is exposed to the claimed stress conditions. Brittain, ¶ 90.

Accordingly, Defendants' respectfully request that the Court adopt their proposed constructions.

5. <u>Disputed Limitations</u>: "the amount of the monosaccharide or disaccharide is such that lanthanum hydroxycarbonate is not observed in an x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate composition after it has been exposed to 60° C. and 95% relative humidity for at least 7 days" (claims 1-12)

Defendants' Proposed Construction	Shire's Proposed Construction
the amount of the monosaccharide or disaccharide present in the lanthanum carbonate composition is such that no lanthanum hydroxycarbonate formed by decarboxylation of the lanthanum carbonate present in the composition is detectable in an x-ray powder diffraction (XRPD) pattern of the composition containing lanthanum carbonate and one or more monosaccharides or disaccharides after the composition has been exposed to 60°C and 95% relative humidity for at least 7 days	the amount of the monosaccharide or disaccharide contained in a lanthanum carbonate composition is sufficient so that lanthanum hydroxycarbonate is not detected through visual inspection by a skilled artisan of x-ray powder diffraction patterns after the composition has been exposed to 60° C. and 95% relative humidity for at least 7 days

As explained immediately above in Section V.A.4, this claim phrase requires the lanthanum carbonate in the composition be "stabilized" by one or more mono- or disaccharides to prevent formation of new "lanthanum hydroxycarbonate" in the composition by decarboxylation *after* the composition is exposed to heat or moisture stressing. Brittain, ¶¶ 85–86, 95. Further, detection of the "lanthanum hydroxycarbonate" formed by decarboxylation is not limited to "visual inspection" of an XRPD pattern – this construction is contrary to the claim language and specification which do not limit detection to "visual inspection." *See Section V.A.4.c.*; Brittain, ¶¶ 91–94.

VI. CONCLUSION

For all of the foregoing reasons, Defendants respectfully request that this Court adopt their proposed claim constructions.

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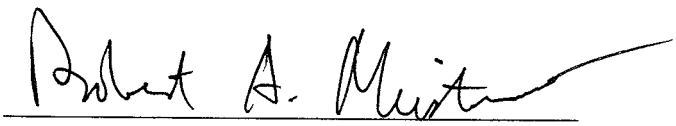

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